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DISCUSSION

H. H. SEARLS, M. D. (University of California Hospital, San Francisco).—The author's paper presents an excellent summary of present-day conceptions of the nodular or adenomatous goiter. That the encapsulated adenoma satisfies all of the pathologic requirements of a true benign tumor still seems evident to many students of thyroid disease. In different endemic regions clinical variations may have modified the picture so as to lead to differing hypotheses concerning its etiology.

The patient with an advanced and neglected toxic adenomatous goiter remains an excellent operative risk, for the mortality rate in the surgical treatment of such patients is almost nil. However, cardiac decompensation should be relieved by bed rest and digitalis therapy. At the University of California Hospital, iodin medication before operation has been limited to patients with the hyperplastic or exophthalmic type of goiter.

X-ray therapy is contraindicated in adenomatous goiter, for such treatment tends to destroy the remaining normal gland tissue without affecting the adenoma.

Doctor Kroger has described adequately the common picture of the patient suffering from toxic goiter together with an associated hypothyroidism. In such instances the lowered metabolism, as shown by increased weight, feeling of cold and lowered basal metabolic rate, offers false reassurance to patient and consultant, whereas the tachycardia, increased irritability and emotionalism accurately betray the underlying toxicity.

When the patient with toxic adenomata exhibits hypertension, removal of the goiter rarely affects the blood pressure other than to check its further rise.

The threat of malignant degeneration is ever present for the patient with nodular goiter, and is the strongest indication for surgical removal of the adenomata.

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CLARENCE G. TOLAND, M. D. (1930 Wilshire Boulevard, Los Angeles).—My thoughts correspond to those of Doctor Kroger. I am especially anxious to emphasize the necessity of considering all adenomas as potential malignancies. Only a small percentage become malignant, it is true, but the conservative attitude of *laissez faire* toward most adenomas is responsible for the occurrence of practically all malignant goiters. In the nineteen-year-old girl cited with the malignant adenoma, no malignancy was suspected before operation. The goiter was removed because of its unsightliness and the knowledge that eventually it would cause trouble. Had we procrastinated until it bothered her, we should have been faced with a hopeless problem. How much less reason is there with middle-aged patients having long-standing adenomas to placate with the philosophy of procrastination.

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WILLIAM E. COSTOLOW, M. D. (Soiland Clinic, Los Angeles).—Toxic adenoma is not as well adapted to roentgen treatment as exophthalmic goiter. In the latter condition it has been shown that about the same percentage of favorable results may be obtained by roentgen treatment as by surgery. However, the results of radiation treatment of toxic adenoma are not nearly as unsatisfactory as this paper indicates. Undoubtedly surgery is the method of choice in the treatment of the majority of toxic adenomas. The operative mortality is very low and the results have been very good. In some cases, however, there may be contraindications to surgical removal. Some patients also refuse operation. If patients with toxic adenomas show a high metabolic rate, radiation may be justifiably used, with the expectation that the metabolism will be reduced to within normal limits in the majority of cases. The adenomatous tumor, however, will not be reduced much in size, if at all. In other words, in toxic adenomas with a high metabolic rate it is possible to reduce the metabolic rate and relieve the toxicity with radiation, although the patient will be left with an adenomatous tumor. If the tumor is small it may be of little consequence afterward, except from a cosmetic standpoint, but if the adenomatous mass is causing pressure symptoms, which frequently is the case, then surgery must be resorted to in order to relieve the patient. In toxic adenomas without pressure symptoms, radiation may be the only treatment that is necessary. In case of failure following radiation treatment, surgery can always be resorted to and the patient will undoubtely be a better surgical risk following the improvement in the toxic symptoms produced by the radiation.

As Doctor Kroger has stated, there is a small danger of malignant degeneration in these tumors. Following radiation treatment the danger must be very small, as Pfahler collected from the literature twelve hundred cases of toxic adenoma which had been treated by radiation methods and did not find a single case in which there was a later development of malignancy.

STERILITY*

REPORT OF SEVEN HUNDRED CONSECUTIVE CASES

By FREDERIC M. LOOMIS, M. D.
Oakland

DISCUSSION *by Margaret Schulze, M. D., San Francisco; Louis I. Breitstein, M. D., San Francisco; Lyle G. McNeile, M. D., Los Angeles.*

NINE years ago the writer had the honor of reporting to this section a study of 150 consecutive cases of sterility. Since then Dr. John W. Sherrick and Dr. James V. Campbell have become associated with him. We now report jointly an analysis of 732 consecutive cases of this type, all private patients in our own office. The writer knows of no greater medical happiness than putting a baby in the arms of a mother who has so longed for one that she has been impelled to come and ask for it, and there are few problems of diagnosis more challenging and more complex.

We have taken fifteen or more facts from the history of each patient, making the appalling number of some fifteen thousand facts to be correlated and interpreted. Many of these facts of history and physical findings have been of little or no value for our specific purpose, though frequently of great value indirectly to the patient,

* Read before the Obstetrics and Gynecology Section of the California Medical Association at the sixty-first annual session, Pasadena, May 2–5, 1932.

as will be shown. We have long felt that fertility is a relative thing, as pointed out by Reynolds and Macomber.

COMPLETE EXAMINATION NECESSARY

It has long been evident that anything less than a reasonably complete and patient series of examinations was quite useless. Nearly every patient had been to her own family doctor at previous times and had been told that he saw no reason why she should not become pregnant. We realize that many women go to their own good doctors who find an eroded cervix or other condition which they are entirely competent to treat, and these women we never see, as their prayers are answered without further help. In a sense, therefore, this group of 732 patients is quite definitely an adversely selected one.

PLAN OF EXAMINATION

It need hardly be stated that the examination consists of four or five parts, somewhat after the Meaker plan, including as a routine an unusually careful history, a complete physical examination of the woman, a Rubin test of passing carbon dioxide gas through the tubes, and a postcoital examination (Huhner) made within about an hour after exposure. To these are added condom examinations, metabolic tests and other determinators as indicated, but we do not include personal examination of the male, pelvic examination under anesthesia, nor other recommended procedures unless definitely demanded by circumstances.

From a practical standpoint for those who are interested in doing this pleasant work, it may be stated that we have found it advisable to make it perfectly clear to the patient before we even take her history that these various examinations are essential, that they must be made before we can tell her one useful fact (except when an impasse is reached before their conclusion), and that we do not want to begin unless she is willing to "carry on" patiently for a considerable time. She is told that as soon as these tests are completed we shall give her a fair opinion as to her prospects, and explicit directions or treatment as needed over a somewhat indefinite time, six months to a year. For this, the patient is told that she will pay a definite inclusive fee which will cover all ordinary treatment, and that this fee, contrary to all other custom in our office, is to be paid in advance. This requirement is based upon the observation that patients who are asked to pay for each procedure as it is advised are likely to say, "Let's wait till next month and perhaps I won't need it then," and this leads to interminable procrastination; and further, we know that when a woman has paid for a thing she is very likely to do as she is told and to come and get it! And results are what we both want.

THE RUBIN TEST

Let us take first the fundamental question of closed or open tubes. The Rubin test is the greatest advance made in many years, as until we had it we so frequently wasted our own time and the patient's money in attempting to do something with a perfectly hopeless patient—hopeless because whatever we might do elsewhere, we could not make her conceive with closed tubes. The importance of this is shown by the fact that only 53 per cent of the 474 patients on whom this test was made had normally patent tubes, 13 per cent being entirely and hopelessly closed after many attempts. Still more interesting is the fact that of the remaining 34 per cent whose tubes, closed on the first trial and partly or completely opened by repeated inflations, nearly 20 per cent, regardless of other conditions, promptly became pregnant. We believe the chief value of the Rubin test is in diagnosis, but in view of these figures it is impossible to deny its therapeutic value also, as pointed out in the excellent recent paper of Stein and Leventhal. In other words, fifty-seven women were saved useless treatment, and about thirty women apparently owe their babies directly to the opening of the tubes by this means. Although the question is frequently raised, we do not encourage the surgical opening of closed tubes, as we cannot promise its permanency, nor that the woman will become pregnant. On the few occasions when the patient has wanted surgery, we have used iodized oil injections and x-ray to determine the points of closure. We use x-ray in this way very infrequently now, feeling that it adds very little to our working knowledge.

THE HUHNER TEST

We find the postcoital examination of the woman of much more importance and interest than the examination of the condom specimen, since it shows the actual condition of the spermatozoa under the hazards to which they are normally subjected. Both are necessary in all questionable cases. Fifty-three per cent of these examinations were normal; that is, there were very numerous spermatozoa, well shaped, active and with normal progressive motion found either in the vaginal pool or in the cervical mucus; 37 per cent were only fair, the number of spermatozoa being markedly decreased or there were defects in form or motion; and in 10 per cent there was a complete aspermia, a practically hopeless condition. A number of these husbands have been under treatment, but only with moderate success and, so far as I know, with no resulting pregnancies. With a little tact it is not difficult to persuade a patient to have these postcoital tests made nor to administer any necessary treatment to the woman; but when the defect is found to be in the man, a great deal of tact is necessary to soften the blow. I suppose all men are convinced that they are born "good," and it is a serious psychic trauma when a man finds that he is not.

The observation of the fate of the spermatozoa in the vaginal and cervical canals is important in many ways. It has been stated frequently that the acidity of the vaginal secretion is of no importance, as it is overcome at once by the alkalinity

of the semen. I cannot agree with this as I have found in several instances every spermatozoön dead in a highly acid vagina, and in the same patient millions of living spermatozoa after intercourse which had been preceded by an alkaline douche; and in several patients pregnancy has immediately resulted with no other treatment. Many times lively spermatozoa will be found in the vaginal pool, but none living can be found in the cervix, either because of a sticky discharge from erosions or, I am convinced, from the dry tenacious mucus so frequently found with cervical stenosis. It has been argued that a cervical canal large enough to afford exit to menstrual blood is large enough to admit spermatozoa. This is quite true; but with a tight cervix, poorly drained of its own mucus, we often find a surface like sticky fly-paper over which the spermatozoa pass with great difficulty, to say the least.

NEW GROWTHS AND INFLAMMATORY TROUBLES

Three per cent of the total number of patients had fibroids or other tumors of sufficient importance to interfere; seven per cent had definite evidence of old inflammatory trouble, some following induced abortion, but only one or two following gonorrhea, a surprisingly small number which is probably explained by the comparatively high type of patient. In several of these, only one side being affected, pregnancy promptly followed surgical removal of the trouble, and we now feel justified in advising such procedure.

MALPOSITION, STENOSIS AND EROSION

Thirty per cent had retroversions, and in 42 per cent there was acute anteflexion with a moderately small fundus. We know that many women with retroversions become pregnant easily, but we usually insert a pessary for trial at least, hoping that we may increase the chances; the anteflexed patients, on the contrary, are most likely to show marked stenosis, perhaps because of underdevelopment, itself an adolescent glandular defect. These patients we usually dilate, using the negative pole of the galvanic current, a simple and inexpensive office procedure. Curettage is never done without specific reason, such as menorrhagia, polyps, or other direct indication. Linear cauterization, however, is done whenever there is cervical erosion of any consequence and the incidence of cervicitis, erosion and excessive discharge is 38 per cent. The results are almost uniformly good.

THE ENDOCRINE QUESTION

And now, finally, a word about the most interesting and most elusive condition of all, the endocrine picture. Sixty-seven per cent of these women were so evidently deficient in this respect that it was at once noted; that is, there were obvious defects in the production of pituitary, thyroid or ovarian secretions. There were some who menstruated only two or three times a year, probably being deficient in all three important glands; some presented typical pictures of hypothyroidism with dry skin and hair, overweight and slow pulse; some had the severe menstrual headaches with nausea, and the so-called pituitary girdle, suggesting deficiency in the anterior pituitary. These would seem particularly amenable to treatment, but as yet only about 35 per cent have become pregnant. Many of these patients presented other problems as well. Two types of preparations have been outstanding, ordinary thyroid pushed at times almost beyond conservative limits and, hypodermatically, the comparatively recent sex hormone products. I recall one girl who flowed frequently and irregularly, bleeding slightly for weeks at a time. We curetted her, found a mild endometrial hyperplasia only, treated her with several of the standard drugs to control bleeding, and the condition was not helped in the least. Finally, though she was a slender girl with a normal metabolic rate, we gave her thyroid in fairly large dosage. The menorrhagia promptly ceased and in a short time pregnancy occurred as desired. We have long felt that the metabolic rate is not the sole criterion of thyroid efficiency, by any means, and indeed it may be deceiving. We are interested in seeing this observation on the part of others, as in the recent publication of Waters and Williams.

We have used the female sex hormone rather empirically and do not see how we can be explicit in our conclusions, as several conditions are almost necessarily being treated at once and judgment is still as difficult as Hippocrates thought it. Unfortunately for speeches at medical conventions, our patients want babies, not statistics, and want them soon. However, there are fifteen or more in this series with whom we had exhausted all our resources who promptly became pregnant when they were called back and given the female sex hormone preparations. We reach a place in the treatment of these girls when everything mechanical has been corrected and we still fail and do not know why—evidently because of biochemical conditions which are still quite beyond our grasp.

There are 732 patients in this series. One hundred and ninety-three of these have not been treated at all, having come too recently to be included fairly in computing results or having not even completed their examinations, leaving 539 who went through the required tests and treatment until successful or until told that pregnancy was unlikely or impossible. Fifteen of this number were dismissed as hopeless because of their husbands' complete aspermia, and fifty-one went no further because repeated trial showed apparently hopelessly closed tubes, leaving 473 who received partial or complete treatment so far as we could give it. Two hundred and eight, or 44 per cent, became pregnant, and from these women we have secured 331 pregnancies and 237 living babies. It is an interesting fact that thirty-six, or 17 per cent, of these who became pregnant suffered involuntary abortions, as if nature were protesting against a pregnancy forced upon her, though thirteen of these eventually went through to term. However, seeking further protests from nature to what might be called an "induced pregnancy" such as these, we find that the incidence of toxemia is

not unusually high, 29 per cent having moderate or severe nausea and only 4 per cent showing late toxemia of some degree, only one instance of eclampsia occurring.

CONCLUSIONS

The histories of 732 consecutive sterility patients are analyzed, of whom 539 completed their examinations and 473 were treated. Of these, 208, or 44 per cent, became pregnant.

Fifty-three per cent gave normal Rubin tests, and 13 per cent were dismissed because repeated efforts showed total closure of tubes. Repeated efforts produced partial or complete opening of the 34 per cent, which were unsatisfactory at first trial, and nearly 20 per cent of these women became pregnant, suggesting the therapeutic value of this procedure.

Fifty-three per cent showed normal spermatozoa after coitus, 37 per cent were only fair, and 10 per cent showed complete aspermia, giving a high percentage of male responsibility in sterility or relative infertility.

Cervical stenosis and erosion were found in 42 per cent and 38 per cent, respectively, and are considered very important causes of failure. Both are amenable to office treatment.

Sixty-seven per cent showed endocrine dysfunction, most of whom were treated with thyroid or preparations of the female sex hormone. Basal metabolism is not relied upon alone in judging hypothyroidism. Thirty-five per cent of these patients became pregnant.

The incidence of toxemia is not higher than normal, but involuntary abortions occurred in 17 per cent.

350 Twenty-ninth Street.

DISCUSSION

MARGARET SCHULZE, M. D. (University of California Hospital, San Francisco).—Doctor Loomis is to be congratulated upon the excellence of his results in a field which has in the past been difficult and often unsatisfactory. Undoubtedly the thoroughness with which he has made his studies and the intelligent coöperation of a superior type of patient in carrying out his treatment have contributed very largely to this success.

The Rubin test has been one of the great advances in the study of these patients and is essential in all cases where the fault has been found to lie with the woman. All authorities are agreed that it has definite therapeutic as well as diagnostic value. Its very simplicity makes it necessary to sound a note of warning to the inexperienced, and to reëmphasize the fact that there are certain contraindications to its use. The main one of these is, of course, the presence of any evidence of infection of the lower genital tract and it is absolutely necessary that any cervical or vaginal discharge be cleared up completely by cautery or other appropriate treatment before the test is undertaken. Because of the theoretical danger of displacement of endometrial fragments through the tube with the possibility of an endometriosis, it is advisable that the test be done only in the early part of the intermenstrual cycle. As Doctor Loomis has stated, the results following plastic operations on closed tubes are not brilliant; yet in an occasional case, where the closure is due to peritubal adhesions and the mucosa remains comparatively normal, success may be obtained. It seems advisable to follow such operations by tubal insufflation.

In the past the greatest success has been obtained in those cases in which it was possible to correct some definite mechanical obstacle, while those in which the sterility was due to constitutional defects the result of endocrine deficiency remained more or less hopeless. The recent great advances in this field make it seem probable that in time we shall develop efficient therapeutic agents here also.

I should like to ask Doctor Loomis whether his statistics confirm the statements of Unterberger, Pfannenstiel, and others, that pregnancy following the use of an alkaline douche in cases where the sterility seemed due to a hyperacidity of vaginal secretion resulted in the production of male offspring only?

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LOUIS I. BREITSTEIN, M. D. (516 Sutter Street, San Francisco).—Doctor Loomis, in his paper on sterility, thought enough of the question of closed tubes to give considerable mention to the Rubin test. He stated that the chief value of the Rubin test was diagnostic, but in view of his statistics the therapeutic value was not to be denied. Interesting in this respect is the fact that thirty of the mothers whose tubes were closed became pregnant when the tubes were completely or partially opened by repeated inflations. Did Doctor Loomis in his experience have any of his cases terminate in tubal pregnancies? One must ever be mindful of this possibility.

Further, fifty-seven women were saved useless treatment, evidently because their tubes were entirely and hopelessly closed even after many attempts with inflation. One must not be altogether too pessimistic in these cases, for considerable tact must be used to "soften the blow" and it is best to leave the question open to time. Time brings about changes even in what appear to be hopelessly closed tubes, and often to our surprise a patient whom we dismissed as hopeless returns pregnant and goes to term. Problems in sterility are ever occurring; not all of them are simple and most are elusive, but Doctor Loomis has presented us with an intelligent and scientific scheme of how they should be attacked.

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LYLE G. MCNEILE, M. D. (Pacific Mutual Building, Los Angeles).—There has been a conspicuous awakening of interest in the problem of sterility during the past decade. While the treatment of sterility is in many instances empirical, the causes have been very well tabulated and recognized, diagnosis has been greatly improved, and great advances in treatment are being made. Doctor Loomis has definitely shown that sterility is not a simple one-sided problem that requires not only a gynecologic history and abdominopelvic examination of the patient, special gynecologic study, medical-endocrine history, examination of both husband and wife, but often a painstaking genitourinary study of the husband. A sterility study which ignores the husband as a possible factor is worthless. Doctor Loomis has pointed out the absolute necessity of requiring patients to submit to a complete study. I, too, am convinced that the Rubin test is of great therapeutic as well as diagnostic value. This paper is timely and complete; it merits the careful study of all obstetricians and gynecologists engaged in sterility studies.

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DOCTOR LOOMIS (Closing).—Contrary to our expectation, we have not yet had an ectopic pregnancy in a sterility patient, although I am sure some of our successful patients have had incompletely patent tubes, the closure probably being near the fimbriated end of the tube. Doctor Schulze asks an interesting question, which I can answer only partially, but the answer is interesting also, though it may not mean much. In a small group of twenty-seven successful patients of high vaginal acidity who were directed to use alkaline douches, there were born nineteen male babies and only eight female.